REMARKS

Claims 1, 60-73 and 79-96 are pending in the application. Claims 1 and 73 are amended. Claims 92-96 are added.

Applicants gratefully acknowledge the reconsideration and withdrawal of the finality of the previous Office Action and the withdrawal of the previous objections and rejections in view of applicants' amendments and remarks in the most recent amendment.

Claim Rejections under §112

Claims 1, 60-73 and 79-91 were rejected under 35 USC 112, first paragraph, for failing to comply with the written description requirement with regard to the recitation of the thickness of the silicon dioxide layer on the aluminum layer. This rejection is respectfully traversed. As noted in the remarks accompanying the previous response, the present inventors have discovered that the presence of a silicon dioxide coating of an appropriate configuration on the aluminum substrate surface can amplify the fluorescent signal used to read the arrays with resultant improvement in performance of the arrays in practice. In particular, the configuration is a thickness of between about 200 and 900Å. While the present application describes several embodiments, some with varying thicknesses of oxide layers, for example at page 21, lines 14-29, this particular embodiment has been found to result in the amplification of a fluorescent signal, is described at page 22, lines 5-14 and in Example 2 at page 36, lines 2-4, an embodiment of the invention to which claims 59 and 78, now canceled, were directed. The independent claims have been further amended to recite the more general characterization of a suitable silicon dioxide coating: configured to amplify a fluorescent signal from a labeled protein bound to the array. Dependent claims 92 and 93, depending from claims 1 and 73 respectively, have been added to recite the oxide thickness range of about 200 to 900Å. In addition, claims 94-96, directed towards a corresponding system incorporating the arrays of the present invention, are added. Both this general characterization and this specific range of a silicon dioxide coating suitable for amplification of a fluorescent signal are clearly described in the specification, in particular in the sections of the specification noted above. Accordingly, in view of these further claim amendments and remarks, it is respectfully submitted that the presently pending claims are in compliance with the written description requirement of 35 U.S.C. §112, first paragraph, and withdrawal of the rejection is respectfully requested.

Claim Rejections under §103

Claims 1, 60, 61, 63-66, 73, 79, 80 and 82-85 were rejected under 35 U.S.C. §103(a) as being unpatentable over US Patent No. 5,478,527 to Gustafson et al. ("Gustafson") in view of US Patent No. 5,831,070 to Pease et al. ("Pease"). Claims 62 and 81 were rejected under 35

U.S.C. §103(a) as being unpatentable over Gustafson and Pease and further in view of US Patent No. 6,406,921 to Wagner et al. ("Wagner"). Claims 67-72 and 86-91 were rejected under 35 U.S.C. §103(a) as being unpatentable over Gustafson and Pease and further in view of US Patent No. 5,482,867 to Barrett et al. ("Barrett").

The present invention is directed to arrays of protein-binding agents stably attached to the surface of a solid support, and kits and systems incorporating such arrays. The arrays, kits and systems are useful for conducting proteomic analyses such as differential binding assays in which the binding of a particular protein to an array element is detected by a fluorescence-based detection system (see, e.g., page 28, line 3 to page 30, line 13 and page 33, line 32 to page 34, line 7). The array is designed to optimize the effectiveness of this fluorescence-based detection system.

The claims have previously been focused on a particular embodiment of the invention in order to expedite prosecution. These claims recite an embodiment of the invention wherein an aluminum on glass substrate surface is coated with a particular configuration of silicon dioxide on the aluminum substrate surface that can amplify the fluorescent signal used to read the arrays with resultant improvement in performance of the arrays in practice. In particular, the configuration is a thickness of between about 200 and 900Å. Claims 1 and 73 have been amended to recite that the solid substrate has a substantially planar surface comprising a layer of aluminum formed on a glass base material, the aluminum coated with a silicon dioxide coating configured to amplify a fluorescent signal from a labeled protein bound to the array, and dependent claims 92 and 93, depending from claims 1 and 73 respectively, have been added to recite the thickness range of about 200 to 900Å. In addition, claims 94-96, directed towards a corresponding system incorporating the arrays of the present invention, are added.

Gustafson discloses and claims a reflective "biograting" composed of an optically flat layer of a transparent composition, such as silicon dioxide, on a reflective metal layer, such as aluminum. The purpose of the grating is to detect a signal from a biomolecule using diffraction as a means of detection. Alternating zones of active and inactive binding reagent are disposed on the optically flat transparent (e.g., silicon dioxide) layer. Gustafson teaches that a silicon dioxide layer between about 100 and 3000Å, and is preferably from about 250 to 1000Å, is suitable for its purposes (col. 6, lines 51-55). In an alternative embodiment, a silicon dioxide layer 800 to 1200Å, and preferably 950-1050Å thick is used in combination with an overlying silicon layer (col. 3, lines 1-14 and col. 10, lines 3-6). The purpose of the optically flat transparent composition (e.g., silicon dioxide) in the Gustafson biograting composition is to provide optimum reflectivity (maximum reflectivity) from the substrate in order to enhance the

diffraction grating signal detectable from the biograting, as described at col. 1, line 51 to col. 2, line 1 and col. 3, line 56 to col. 4, line 5. This is a label-free method of detection; a completely different method of detection (diffraction) from that for which the arrays of the present invention are configured (fluorescence). Accordingly, Gustafson provides no teaching with regard to a fluorescence-based detection system or an array of protein binding agents configured and optimized for conducting assays using fluorescence-based detection. As noted by the Examiner, Gustafson also does not teach protein binding agents with peptidomimetic segments.

Pease discloses arrays of polymers, including peptidomimetics, disposed on a solid support. However, Pease does not teach or suggest a substrate composed of aluminum coated with silicon dioxide. And while Pease does disclose a fluorescence-based detection system, it provides no teaching or suggestion with regard to the optimization of that system by an array configured for amplification of the fluorescence signal in accordance with the present invention. Similarly, while Wagner and Barrett disclose other aspects of the protein binding agents claimed in dependent claims in the present application, neither of these references addresses the deficiency of Pease with regard to the optimization of the array configuration for amplification of the fluorescence signal in accordance with the present invention.

In view of the foregoing, it is respectfully submitted that one of skill in the art would not be led to combine Gustafson and Pease, and further combine those references with Wagner and/or Barrett to achieve the presently claimed invention. Nor would the combination suggested by the Examiner achieve the present invention. This is because the fundamental basis for the selection of the particular combination of aluminum coated with silicon dioxide configured as presently claimed is to amplify the fluorescent signal detectable from the array in use. Gustafson incidentally discloses a range of silicon dioxide thicknesses for its substrate that includes the range presently claimed for this configuration. However, since Gustafson uses a completely different label free detection system, there is no motivation to substitute the peptidomimetic protein binding agents with their associated fluorescence-based detection system into the Gustafson biograting.

Moreover, such a combination would not would not achieve the present invention since each of the protein-binding agent array elements of the presently claimed invention comprises a peptidomimetic protein-binding segment configured to potentially bind a protein. To the contrary, a substantial proportion of the array elements of Gustafson are explicitly inactive, having been specifically deactivated so that they do not bind in order to form the biograting.

Similarly, there is no motivation provided to a reader of Pease to substitute the silicon dioxide coated aluminum substrate of Gustafson for its own substrate since there is nothing in either reference to suggest a benefit in doing so, and certainly not the possibility that

amplification of the fluorescent signal from the Pease array might be possible using the Gustafson substrate since Gustafson is not at all concerned with fluorescent signal amplification.

As noted above, independent claims 1 and 73 of the present application have been amended or drafted to recite that the array substrate comprises a silicon dioxide configured to amplify a fluorescent signal from a labeled protein bound to the array. In addition, claims 92 and 93 have been added to recite the limitation previously presented claims 59 and 83 and then 1 and 73, namely that the silicon dioxide has a thickness between 200 and 900Å. In addition, claims 94-96, directed to a corresponding system, have been added. These amendments are supported by the specification, in particular at page 22, lines 5-14, in Example 2 at page 36, lines 2-4, at page 28, line 3 to page 30, line 13 and at page 33, line 32 to page 34, line 7. Thus no new subject matter is claimed by these amendments. These amendments are made without prejudice to further prosecution of the subject matter of any cancelled claim in this or a subsequently filed continuation or divisional application.

For at least these reasons, it is respectfully submitted that claim1, and corresponding kit claim 73, and system claim 94 of the present application are novel and patentable over the cited references. The remaining pending claims depend, directly or indirectly, from claim 1, 73 or 94 and are thus submitted to be patentable for at least the same reasons. Thus, withdrawal of the rejections under 35 U.S.C. §103(a) is respectfully requested.

Other Amendments

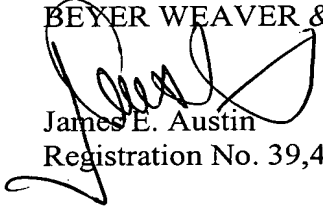
The claims have also been amended to correct any formal issues, where noted. And claim 73 has been amended to further recite that the kit further comprises differential binding assay reagents to clarify that which is claimed.

Conclusion

Applicants believe that all pending claims are allowable and respectfully request a Notice of Allowance for this application from the Examiner. Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be reached at the telephone number set out below. If any additional fees are due in connection with

the filing of this amendment, the Commissioner is authorized to charge such fees to Deposit Account 500388 (Order No. CHIRP014).

Respectfully submitted,
BEYER WEAVER & THOMAS, LLP



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